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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Rec'd PCT/PTO 11 FEB 2005

Applicant's or agent's file reference 2K/2AM05/MJ/4	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/09009	International filing date *(day/month/year)* 12.08.2003	Priority date *(day/month/year)* 12.08.2002
International Patent Classification (IPC) or both national classification and IPC C01B33/12		
Applicant BIO MINERALS N.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10.03.2004	02.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Rhodes, K Telephone No. +49 89 2399-8259

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/09009

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-10 as originally filed

Claims, Numbers

1-14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. **Reference is made to the following documents:**

D1: EP-A-1110909
D2: US-A-5922360
D3: US-B1-6335457

2. **Novelty**

Document D1 discloses a method for the preparation of orthosilicic acid adsorbed on a particulate carrier, obtainable by a process comprising the following steps: (I) providing a solution, comprising orthosilicic acid stabilized with an acid solvent agent; and (ii) contacting the orthosilicic acid comprising solution with a particulate carrier. The carrier, after contact with the orthosilicic acid, is extruded (page 3, lines 11-19).
The orthosilicic acid is formed by hydrolysing a silicon compound in an acid solution, in the presence of a solvent agent (page 2, lines 24-26). The acid solvent agent is selected from a group comprising glycol, glycerol, (poly)alkylene glycol, DMSO and polysorbate 80 (page 2, line 54). Suitable solid carriers include cellulose or its derivatives, sugars or their derivatives. starch and derivatives thereof, and natural and semi-synthetic fibres (paragraph [0015]).
Example B shows the mixing of 65% of a microcrystalline cellulose carrier with 35% of the stabilized orthosilicic acid mixture, which is equivalent to a loading capacity of 35%. The loading capacity can be increased to 45% orthosilicic acid.

Document D2 discloses a method for preparing a preparation comprising stabilized orthosilicic acid, said method comprising: (I) providing a solution containing a stabilizing agent, (ii) dissolving an inorganic silicon compound in said solution, and (iii) hydrolysing the silicon compound to orthosilicic acid (column 1, lines 36-46). Suitable stabilizing agents include quaternary ammonium compounds such as choline, and amino acids such as proline and serine (column 1, line 59 - column 2, line 7.

Sugar/maltose may be used as solid carrier, enabling tablets and gels to be

formed from the orthosilicic acid comprising preparation (column 2, lines 63-67).

The subject-matter of claim 1 differs mainly from the disclosure of document D1, in that the stabilizing agent employed is a quaternary ammonium compound, or an amino acid, or an amino acid source or combinations thereof.

The subject-matter of claim 1 differs mainly from the disclosure of document D2, in that the preparation of the prior art document is subsequently mixed with a carrier, in an amount up to the loading capacity of said carrier, and the produced mass is then extruded to arrive at the presently claimed method.

As the method of the present application differs from both that of D1 and that of D2, the subject-matter of **claim 1** and dependent **claims 2-11** is novel (Article 33(2) PCT).

Claim 12 is a so-called "product-by-process" claim. To enable comparison with, and differentiation from, the products of the prior art, claims to products should, where possible, be defined in terms of their product features as opposed to the features of their process of manufacture. However, it is thought that the extrudate of claim 12 will comprise the stabilizing agent employed in the process. The use of the stabilizing agent of the present application is not known from D1. Nor is the loading of the silicic acid preparation onto a carrier, followed by extrusion of the produced mass, known from D2. **Claims 12 and 13** are therefore considered to be novel.

Claim 14 concerns a pharmaceutical composition comprising the extrudate according to claim 12. As the extrudate of claim 12 is novel, the pharmaceutical composition comprising said extrudate must also be novel.

3. Inventive Step

The problem to be solved by the present application may be seen as how to provide an extrudate comprising bioavailable silicic acid, and a method for its production.

It is thought to be obvious for the person skilled in the art to combine the teachings of D1, namely loading a suitable carrier with stabilized silicic acid and

extruding the resultant mixture, with the teachings of D2, namely employing quaternary ammonium compounds or amino acids as the stabilizing agent, to arrive at the process of present claim 1. Furthermore, as no surprising effects are demonstrated by combining the stabilizing agents of D2 with the process of D1, the subject-matter of **claim 1** is not inventive in the sense of Article 33(3) PCT.

Document D3 discloses a method for preparing a complex containing biologically assimilable orthosilicic acid, in which the orthosilicic acid is complexed with a polypeptide and is under solid, stable and concentrated form. Said method comprises the addition of a water soluble alcohol to a pH adjusted, aqueous polypeptide solution, followed by the dropwise addition of a hydrolysable precursor of orthosilicic acid. The mixture is then stirred until hydrolysis of the precursor is completed, and the water and alcohol are subsequently removed by evaporation. The polypeptide employed is preferably a hydrolysate of proteins from animal or vegetable origin (column 3, lines 11-34).

The features of dependent claims 2-5 are seen in D2 and D3 and are thought to be merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed, in combination with the teachings of D1. Thus, **claims 2-5** are not inventive.

Claim 6 is concerned with the silicon, choline and water content of the prepared, stabilised silicic acid. This feature is seen in D2 (column 3, lines 25-27), where the obtained preparation contains 3% silicon by weight, 70% choline hydrochloride by weight and 27% water by weight. Therefore, **claim 6** is rendered not inventive.

In D1, Example B, it is shown that 65% of the microcrystalline cellulose carrier is mixed with 35% of the stabilized orthosilicic acid. The loading capacity of the carrier for the stabilized orthosilicic acid is 35% and may be increased to 45%. The mixture is extruded and the extruded strands are spheronized. Typically, the resulting pellet size is between 800 and 1200 µm. As these features are present in D1, it is a clear indication to the skilled person to incorporate them into a process such as that of the present application.
Thus, **claims 7-11** are not thought to be inventive.

Although the extrudate of **claim 12** is novel over the prior art, due to the fact that it will comprise the stabilizing agent employed in the process, and the use of the

stabilizing agent of the present application is not known from the method of D1, the claim is not inventive for the following reason: The combination of the methods of D1 and D2 is deemed an obvious decision by the skilled person, and the extrudate of the product thus formed shows no unexpected technical effect.

Claim 13 relates to the extrudate of claim 12, although certain uses of said extrudate are stipulated. However, claims 12 and 13 are thought to refer to the same subject-matter as they both relate to the extrudate, and not to any specific uses thereof. Thus, as the extrudate of claim 12 is not inventive, neither can the extrudate of claim 13 be inventive.

However, it should be borne in mind that in the event that claim 13 is amended such that it becomes a use claim, the use of such extrudates for the production of animal feed, food, food supplements, and cosmetic or pharmaceutical preparations is not inventive, as the use of such extrudates for these purposes is known from D1 (see, for instance, claim 14). Furthermore, it is acknowledged that such extrudates will have a positive effect on nails, hair, skin, teeth, collagen, connective tissue, bones, will encourage cell generation and inhibit degenerative (ageing) processes (page 3, lines 23-27).

The pharmaceutical composition of **claim 14**, comprising the extrudate according to claim 12, is not inventive as pharmaceutical compositions of this type are known in the art (see D1, Example F, where capsules of the preparation of example D have been produced), and it is obvious to the skilled person to produce such compositions from extrudates such as that of the present application.

4. Industrial Applicability

The silicic acid comprising extrudate of the present application is of clear industrial applicability in fields such as cosmetic and pharmaceutical preparations, animal feed and food supplements.